```
FILE 'REGISTRY' ENTERED AT 15:46:28 ON 20 OCT 2003
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STRUCTURE FILE UPDATES:   19 OCT 2003  HIGHEST RN 606921-26-0
DICTIONARY FILE UPDATES:  19 OCT 2003  HIGHEST RN 606921-26-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10066356.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SEARCH INITIATED 15:47:03 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      1 TO ITERATE

100.0% PROCESSED       1 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            1 TO       80
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 15:47:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     38 TO ITERATE

100.0% PROCESSED      38 ITERATIONS  (     3 INCOMPLETE)        4 ANSWERS
SEARCH TIME: 00.00.01

L3            4 SEA SSS FUL L1

=> file caplus
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.15	148.36

FILE 'CAPLUS' ENTERED AT 15:47:16 ON 20 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Oct 2003 VOL 139 ISS 17
FILE LAST UPDATED: 19 Oct 2003 (20031019/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 7 L3

=> s l4/prep
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a field code. You can only add a field code to a term that has no field code appended to it.

=> s l4 and prep?
L5 4 L4 AND PREP?

=> d ibib abs hitstr tot

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:615581 CAPLUS
DOCUMENT NUMBER: 137:154951
TITLE: Preparation and purification of antiviral disulfonic acid disodium salt
INVENTOR(S): Iera, Silvio; Demerson, Christopher Alexander; Lunetta, Jacqueline Francesca; MacEwan, Michael Francis; McMahon, Wayne Gregory; Mohan, Arthur G.; Papamichelakis, Maria; Potoski, John Richard
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062769	A2	20020815	WO 2002-US2933	20020131
WO 2002062769	A3	20030424		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

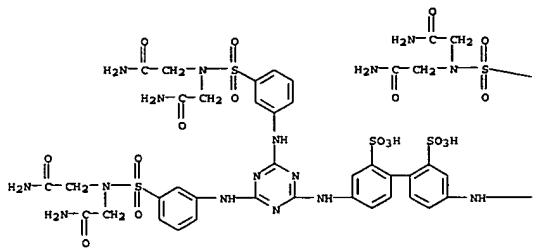
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002151548	A1	20021017	US 2002-66356	20020131

PRIORITY APPLN. INFO.: US 2001-266124P P 20010202
OTHER SOURCE(S): CASREACT 137:154951
AB The antiviral compd. 4',4-bis[4,6-bis[3-[bis(carbamoyl)methyl-1-sulfamoyl]phenylamino][1,3,5]triazin-2-ylamino]biphenyl-2,2'-disulfonic acid and its pharmaceutically acceptable salts is prepd. by (a) reacting 2-(3-nitrobenzenesulfonylamino)acetamide with ClCH2CONH2 in the presence of N,N-dimethylformamide and a base to form 2-[carbamoylmethyl(3-nitrobenzenesulfonyl)amino]acetamide; (b) treating the 2-[carbamoylmethyl(3-nitrobenzenesulfonyl)amino]acetamide with a reducing agent to form 2-[(3-Aminobenzenesulfonyl)carbamoylmethylamino]acetamide; (c) treating the 2-[(3-aminobenzenesulfonyl)carbamoylmethylamino]acetamide with cyanuric chloride to give 2-[[4-[4-[4-(Bis-carbamoylmethylsulfamoyl)benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl]benzenesulfonyl]carbamoylmethylamino]acetamide; and (d) reacting the 2-[[4-[4-[4-[bis(carbamoylmethyl)sulfamoyl]benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl]benzenesulfonyl]carbamoylmethylamino]acetamide with disodium salt of 4,4'-diamino-2,2'-biphenyldisulfonic acid.
IT 197366-24-8P
RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. and purifn. of antiviral disulfonic acid disodium salt)
RN 197366-24-8 CAPLUS

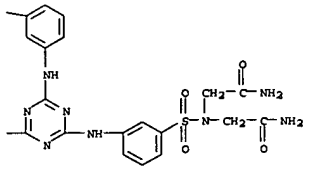
L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



●2 Na

PAGE 1-B

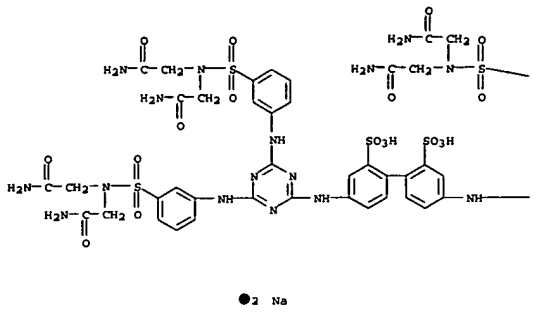


L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

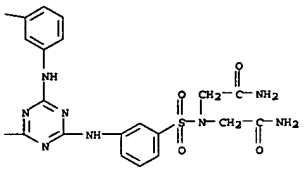
L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:505090 CAPLUS
DOCUMENT NUMBER: 136:95595
TITLE: RFI-641 inhibits entry of respiratory syncytial virus via interactions with fusion protein
AUTHOR(S): Razinkov, V.; Gazumyan, A.; Nikitenko, A.; Ellestad, G.; Krishnamurthy, G.
CORPORATE SOURCE: Department of Biological Chemistry, Wyeth-Ayerst Research, Pearl River, NY, 10965, USA
SOURCE: Chemistry & Biology (2001), 8(7), 645-659
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: RFI-641, a small dendrimer-like compd., is a potent and selective inhibitor of respiratory syncytial virus (RSV), which is currently a clin. candidate for the treatment of upper and lower respiratory tract infections caused by RSV. RFI-641 inhibits RSV growth with an IC50 value of 50 nM and prevents syncytia formation in tissue culture. RSV contains of three surface glycoproteins, a small hydrophobic (SH) protein of unknown function, and attachment (G) and fusion (F) proteins that enable binding and fusion of virus, resp., with target cells. Because of their role in attachment and fusion, the G and F surface proteins are prominent targets for therapeutic intervention. RFI-641 was previously shown to bind purified prepns. of RSV fusion protein. Based on this observation, in conjunction with the biol. results, it was speculated that the fusion event might be the target of these inhibitors. Results: A fusion assay based upon the relief of self-quenching of octadecyl rhodamine R18 was used to det. effects of the inhibitors on binding and fusion of RSV. The results show that RFI-641 inhibits both RSV-cell binding and fusion events. The inhibition of RSV is mediated via binding to the fusion protein on the viral surface. A closely related analog, WAY-158830, which is much less active in the virus-infectivity assay does not inhibit binding and fusion of RSV with Vero cells. Conclusions: RFI-641, an in vivo active RSV inhibitor, is shown to inhibit both binding and fusion of RSV with cells, events that are early committed steps in RSV entry and pathogenicity. The results described here demonstrate that a non-peptidic, small mol. can inhibit binding and fusion of enveloped virus specifically via interaction with the viral fusion protein.
IT 197366-24-8, RFI 641
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RFI 641; RFI-641 inhibits entry of respiratory syncytial virus via interactions with fusion protein)
RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



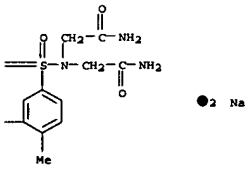
PAGE 1-B



IT 388631-62-7, WAY 158830
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RPI-641 inhibits entry of respiratory syncytial virus via interactions
with fusion protein)

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

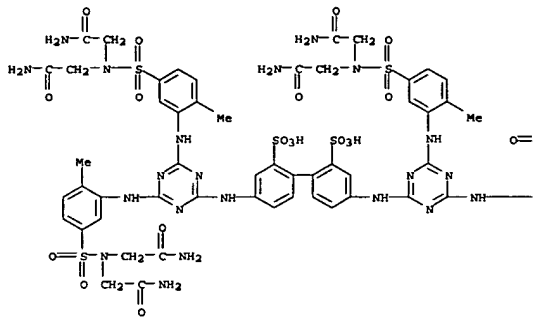
PAGE 1-B



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
RN 388631-62-7 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[5-[[bis(2-amino-2-
oxoethyl)amino]sulfonyl]-2-methylphenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:769193 CAPLUS
DOCUMENT NUMBER: 128:88933
TITLE: **Preparation** of triazine-containing anionic compounds and their use as antiviral agents
INVENTOR(S): Gluzman, Yakov; Larocque, James Paul; O'Hara, Bryan Mark; Morin, John Edward; Ellestad, George Alfred; Mitsner, Boris; Ding, Wei Dond; Raifekd, Yuri Efimovich; Nikitenko, Antonina Aristotelev
PATENT ASSIGNEE(S): American Cyanamid Co., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09309882	A2	19971202	JP 1997-28029	19970212
US 5852015	A	19981222	US 1997-789038	19970127
SK 282598	B6	20021008	SK 1997-179	19970206
NO 9700652	A	19970814	NO 1997-652	19970212
CA 2197394	AA	19980727	CA 1997-2197394	19970212
IL 120206	A1	20000217	IL 1997-120206	19970212
RU 2170731	C2	20010720	RU 1997-102335	19970212
CZ 290450	B6	20020717	CZ 1997-423	19970212
NZ 328399	A	20010427	NZ 1997-328399	19970723
PRIORITY APPLN. INFO.:			US 1996-11542P P	19960213
			US 1997-789038 A	19970127

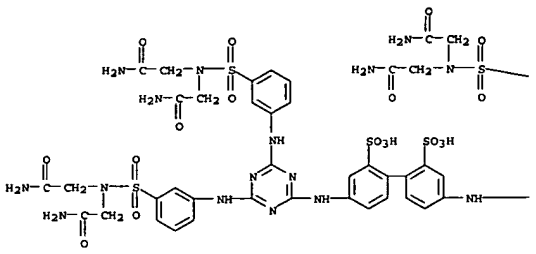
OTHER SOURCE(S): MARPAT 128:88933
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The compds. I [A = II, III, IV, V, VI, VII; R = SO3H, OSO3H, OH, CO2H; B = NH, NR1; R1 = C1-6 alkyl which may be substituted with Cl, Br, F, OH, cyano; X = Cl, F, VIII; U = SO2, CO, NCO, NCS; W = N(YZ)2, IX, X; Y = C(CH2)n; n = 0-6; m = 0-2; Z = H, Me, CF3, CH2X, CH2OH, CO2H, C1-6 alkoxycarbonyl, CONR22, cyano, CHR2OH; X = Cl, Br, F, I; R2 = H, C1-6 alkyl], their salts, or their esters are claimed. Also claimed are pharmaceutical compns. contg. .gtoreq.1 I, their salts, or their esters for treatment of infection with respiratory syncytial virus (RSV), herpes simplex virus, HIV virus, cytomegalovirus, and influenza virus. 4,4'-Bis[4,6-di[3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimino]-1,3,5-triazin-2-ylamino]stilbene-2,2'-disulfonic acid, prepd. from cyanuric chloride, 4,4'-diaminostilbene-2,2'-disulfonic acid, and 3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimine, inhibited plaque formation of RSV in Vero cells at IC50 0.1 .mu.g/mL. A small-particle aerosol of this compd. also showed antiviral effect on cotton rats infected with RSV.
IT 197366-24-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
(prepn. of triazine-contg. anionic compds. as antiviral agents)
RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

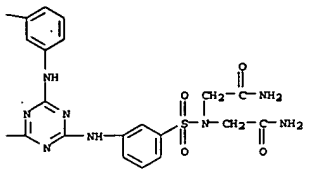
PAGE 1-A



●2 Na

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

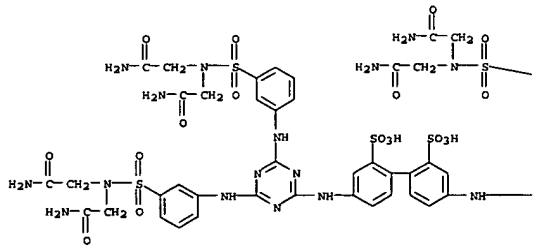
ACCESSION NUMBER: 1997:632410 CAPLUS
DOCUMENT NUMBER: 127:307402
TITLE: Preparation of bis-aryloxy(amino)-triazinyl-oxy(amino)aryl derivatives as antiviral agents
INVENTOR(S): Gluzman, Yakov; Larocque, James Paul; O'Hara, Bryan Mark; Morin, John Edward; Ellestad, George Alfred; Mitsner, Boris; Ding, Wei-Dong; Raifeld, Yuri Efimovich; Nikitenko, Antonina Aristotelev
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 795549	A1	19970917	EP 1997-300905	19970212
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5852015	A	19981222	US 1997-789038	19970127
SK 282598	B6	20021008	SK 1997-179	19970206
NO 9700652	A	19970814	NO 1997-652	19970212
CA 2197394	AA	19980727	CA 1997-2197394	19970212
IL 120206	A1	20000217	IL 1997-120206	19970212
RU 2170731	C2	20010720	RU 1997-102335	19970212
CZ 290450	B6	20020717	CZ 1997-423	19970212
NZ 328399	A	20010427	NZ 1997-328399	19970723

PRIORITY APPLN. INFO.: US 1996-11542P P 19960213
US 1997-789038 A 19970127
OTHER SOURCE(S): MARPAT 127:307402
GI

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
derivs. as antiviral agents)
RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

PAGE 1-A

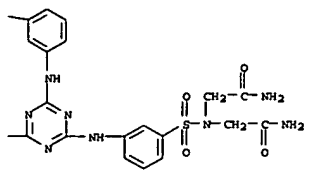


●2 Na

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = II, III, etc.; C' = SO3H, OSO3H, OH, COOH; B' = NH, NH, N(C1-6 alkyl); X = Cl, F, IV; U' = SO2, CO, NC(O), NC(S); W' = N(YZ), V, VI; Y = (CH2)n; n = 0-6; m = 0-2; Z = H, CH3, CF3, etc.] and their salts, useful as pharmaceuticals, esp. for treating viral infections, particularly infections by respiratory syncytial virus, herpes simplex virus, human immunodeficiency virus, and cytomegalovirus, were prepd. Thus, reaction of cyanuric chloride with 4,4'-diaminostilbene-2,2'-disulfonic acid in the presence of NaOH in dioxane/phosphate buffer soln. followed by addn. of 3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimine in DMSO afforded 72% I.2Na+ [A = II; C' = H; B' = NH; X = IV; U'W' = 3-SO2N[(CH2)2CONH2]2] which showed IC50 of 0.3 .mu.G/mL against respiratory syncytial virus growth.
IT 197366-24-8P 197366-84-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis-aryloxy(amino)-triazinyl-oxy(amino)aryl

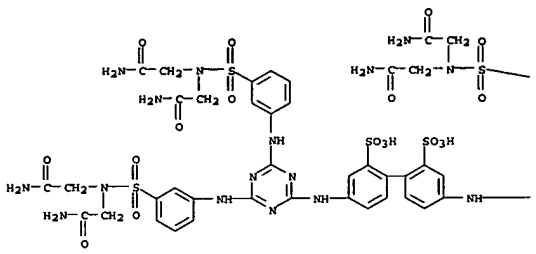
PAGE 1-B



RN 197366-84-0 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, ...is(2-amino-2-

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]- (9CI)
(CA INDEX NAME)

PAGE 1-A



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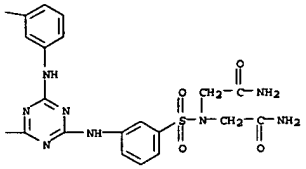

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L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

AB The antiviral compd. 4',4-bis[4,6-bis[3-[bis(carbamoyl)methyl-1-sulfamoyl]phenylamino][1,3,5]triazin-2-ylamino]biphenyl-2,2'-disulfonic acid and its pharmaceutically acceptable salts is prepd. by (a) reacting 2-(3-nitrobenzenesulfonylamino)acetamide with ClCH2CONH2 in the presence of N,N-dimethylformamide and a base to form 2-[carbamoylmethyl(3-nitrobenzenesulfonyl)amino]acetamide; (b) treating the 2-[carbamoylmethyl(3-nitrobenzenesulfonyl)amino]acetamide with a reducing agent to form 2-[(3-Aminobenzenesulfonyl)carbamoylmethylamino]acetamide; (c) treating the 2-[(3-aminobenzenesulfonyl)carbamoylmethylamino]acetamide with cyanuric chloride to give 2-[[4-[4-[4-(Bis-carbamoylmethylsulfamoyl)benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl]benzenesulfonyl]carbamoylmethylamino]acetamide; and (d) reacting the 2-[[4-[4-[4-[bis(carbamoylmethyl)sulfamoyl]benzyl]-6-chloro-[1,3,5]triazin-2-ylmethyl]benzenesulfonyl]carbamoylmethylamino]acetamide with disodium salt of 4,4'-diamino-2,2'-biphenyldisulfonic acid.

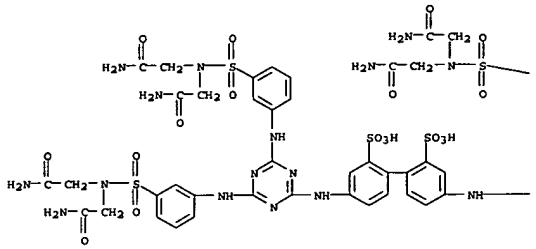
IT 197366-24-8P

RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. and purifn. of antiviral disulfonic acid disodium salt)

RN 197366-24-8 CAPLUS

CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

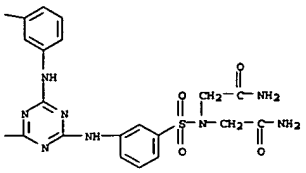
PAGE 1-A



●2 Na

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

AB RSV (respiratory syncytial virus) fusion is mediated by F-protein, a major viral surface glycoprotein. CL-309623, a specific inhibitor of RSV, interacts tightly with F-protein, which results in a hydrophobic environment at the binding site. The binding is selective for F-protein and does not occur with G-protein, a surface glycoprotein that facilitates the binding of RSV to target cells, or with lipid membranes at concns. in the sub-millimolar range. Using an assay based on the relief of self-quenching of octadecyl rhodamine (R18) incorporated in the RSV envelope, the authors show that the virus fuses efficiently with large unilamellar vesicles contg. cholesterol, in the absence of specific receptor analogs. Fusion of cp-52, a mutant virus lacking the G and SH surface glycoproteins, with vesicles is inhibited by CL-309623 and RFI-641 due to specific interactions of the inhibitor(s) with the fusion protein. Both virus-vesicle and virus-cell fusion are inhibited with equal potency. The formation of the binary complex of CL-309623 with F-protein in its native state, resulting in the inhibition of fusion and entry of virus, is a prerequisite for the obsd. anti-RSV activity in cell cultures.

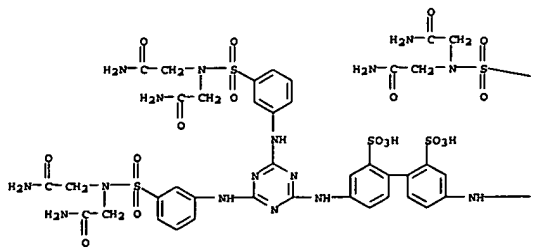
IT 197366-24-8, RFI-641

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(respiratory syncytial virus (RSV) entry inhibitors block F-protein mediated fusion with model membranes)

RN 197366-24-8 CAPLUS

CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

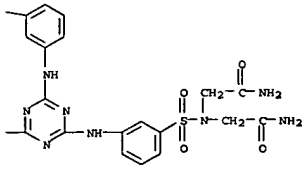
PAGE 1-A



●2 Na

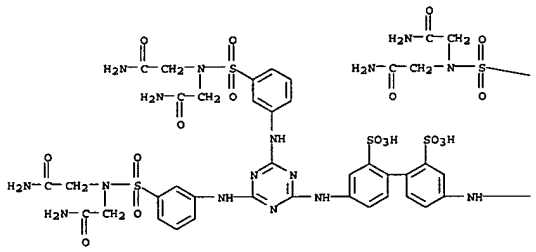
L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AB Human respiratory syncytial virus (RSV), a paramyxovirus, is a major cause of acute upper and lower respiratory tract infections in infants, young children, and adults. RFI-641 is a novel anti-RSV agent with potent in vitro and in vivo activity. RFI-641 is active against both RSV type A and B strains. The viral specificity and the large therapeutic window of RFI-641 (> 100-fold) indicate that the antiviral activity of the compd. is not due to adverse effects on normal cells. The potent in vitro activity of RFI-641 can be translated to efficacy in vivo: RFI-641 is efficacious when administered prophylactically by the intranasal route in mice, cotton rats, and African green monkeys. RFI-641 is also efficacious when administered therapeutically (24 h postinfection) in the monkey model. Mechanism of action studies indicate that RFI-641 blocks viral F protein-mediated fusion and cell syncytium formation.
IT 197366-24-8, RFI 641
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RFI 641; RFI-641 is a potent respiratory syncytial virus inhibitor)
RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

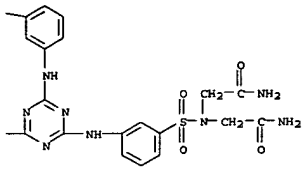
PAGE 1-A



●2 Na

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

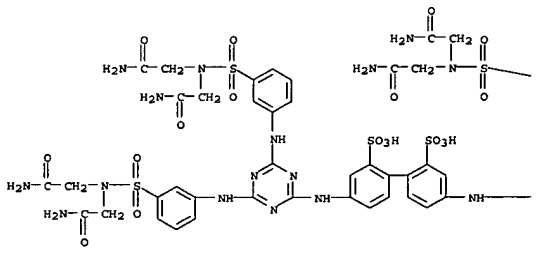
PAGE 1-B



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AB Background: RFI-641, a small dendrimer-like compd., is a potent and selective inhibitor of respiratory syncytial virus (RSV), which is currently a clin. candidate for the treatment of upper and lower respiratory tract infections caused by RSV. RFI-641 inhibits RSV growth with an IC50 value of 50 nM and prevents syncytia formation in tissue culture. RSV contains of three surface glycoproteins, a small hydrophobic (SH) protein of unknown function, and attachment (G) and fusion (F) proteins that enable binding and fusion of virus, resp., with target cells. Because of their role in attachment and fusion, the G and F surface proteins are prominent targets for therapeutic intervention. RFI-641 was previously shown to bind purified prepns. of RSV fusion protein. Based on this observation, in conjunction with the biol. results, it was speculated that the fusion event might be the target of these inhibitors. Results: A fusion assay based upon the relief of self-quenching of octadecyl rhodamine R18 was used to det. effects of the inhibitors on binding and fusion of RSV. The results show that RFI-641 inhibits both RSV-cell binding and fusion events. The inhibition of RSV is mediated via binding to the fusion protein on the viral surface. A closely related analog, WAY-158830, which is much less active in the virus-infectivity assay does not inhibit binding and fusion of RSV with Vero cells. Conclusions: RFI-641, an in vivo active RSV inhibitor, is shown to inhibit both binding and fusion of RSV with cells, events that are early committed steps in RSV entry and pathogenicity. The results described here demonstrate that a non-peptidic, small mol. can inhibit binding and fusion of enveloped virus specifically via interaction with the viral fusion protein.
IT 197366-24-8, RFI 641
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RFI 641; RFI-641 inhibits entry of respiratory syncytial virus via interactions with fusion protein)
RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

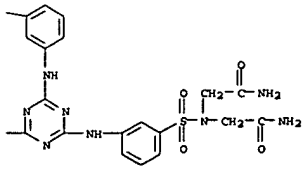
L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



●2 Na

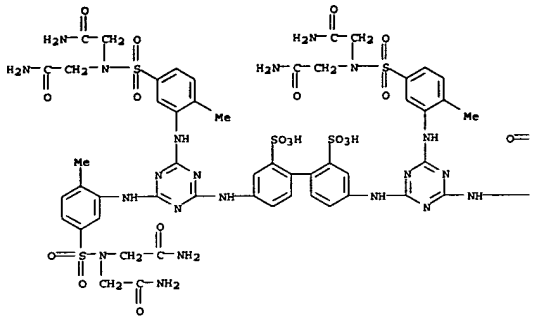
PAGE 1-B



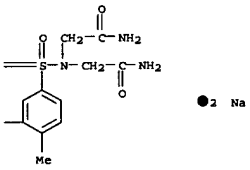
IT 388631-62-7, WAY 158830
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RFI-641 inhibits entry of respiratory syncytial virus via interactions with fusion protein)
RN 388631-62-7 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[5-[[bis(2-amino-2-oxoethyl)amino]-2-methylphenyl]amino]-1,3,5-triazin-2-yl]amino]-,

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)
disodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

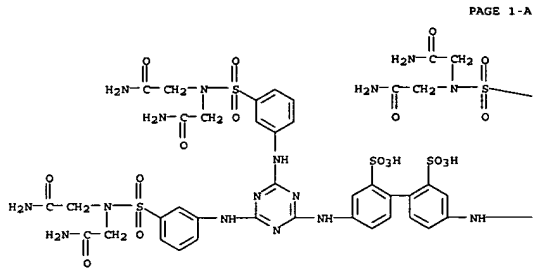
AB The design and synthesis of a new potent and selective inhibitor of the respiratory syncytial virus are described. This compd., RFI-641, emerged from anal. of the structure-activity relationship in a series of biphenyl triazine anionic compds. possessing specific anti-RSV activity. RFI-641 inhibited RSV in vitro and in vivo models.

IT 197366-24-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of RFI-641 as inhibitor of respiratory syncytial virus)

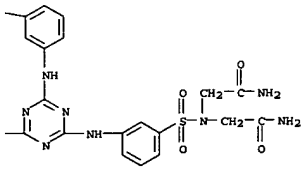
RN 197366-24-8 CAPLUS

CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

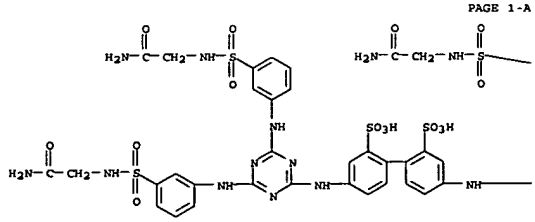
PAGE 1-B

IT 350799-02-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of RFI-641 as inhibitor of respiratory syncytial virus)

RN 350799-02-9 CAPLUS

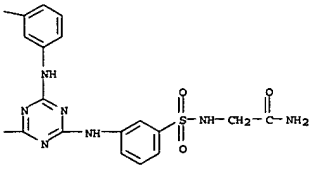
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-B



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

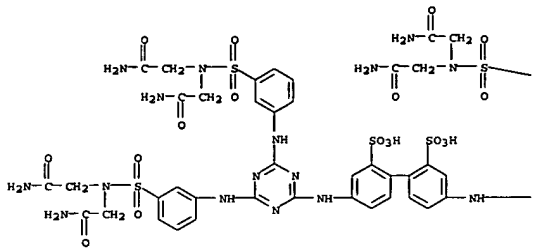
AB The compds. I [A = II, III, IV, V, VI, VII; R = SO3H, OSO3H, OH, CO2H; B = NH, NR1; R1 = C1-6 alkyl which may be substituted with Cl, Br, F, OH, cyano; X = Cl, F, VIII; U = SO2, CO, NCO, NCS; W = N(YZ)2, IX, X; Y = C(CH2)n; n = 0-6; m = 0-2; Z = H, Me, CF3, CH2X, CH2OH, CO2H, C1-6 alkoxycarbonyl, CONR22, cyano, CHR2OH; X = Cl, Br, F, I; R2 = H, C1-6 alkyl], their salts, or their esters are claimed. Also claimed are pharmaceutical compns. contg. .gtoreq.1 I, their salts, or their esters for treatment of infection with respiratory syncytial virus (RSV), herpes simplex virus, HIV virus, cytomegalovirus, and influenza virus. 4,4'-Bis[4,6-di[3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimino]-1,3,5-triazin-2-ylamino]stilbene-2,2'-disulfonic acid, prepd. from cyanuric chloride, 4,4'-diaminostilbene-2,2'-disulfonic acid, and 3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimine, inhibited plaque formation of RSV in Vero cells at IC50 0.1 .mu.g/mL. A small-particle aerosol of this compd. also showed antiviral effect on cotton rats infected with RSV.

IT **197366-24-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of triazine-contg. anionic compds. as antiviral agents)

RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

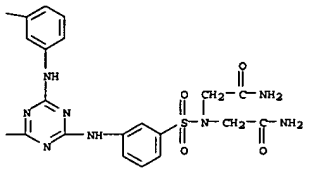
L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



●2 Na

PAGE 1-B



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

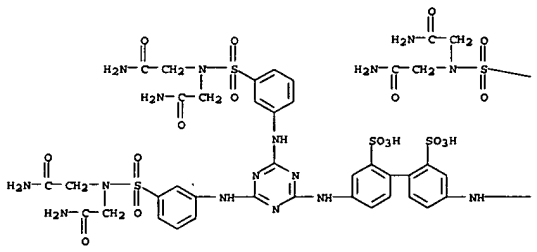
AB The title compds. [I; A = II, III, etc.; C' = SO3H, OSO3H, OH, COOH; B' = NH, NH, N(C1-6 alkyl); X = Cl, F, IV; U' = SO2, CO, NC(O), NC(S); W' = N(YZ), V, VI; Y = (CH2)n; n = 0-6; m = 0-2; Z = H, CH3, CF3, etc.] and their salts, useful as pharmaceuticals, esp. for treating viral infections, particularly infections by respiratory syncytial virus, herpes simplex virus, human immunodeficiency virus, and cytomegalovirus, were prepd. Thus, reaction of cyanuric chloride with 4,4'-diaminostilbene-2,2'-disulfonic acid in the presence of NaOH in dioxane/phosphate buffer soln. followed by addn. of 3-aminophenyl-N,N-bis(2-carbamoylethyl)sulfonylimine in DMSO afforded 72% I.2Na+ {A = II; C' = H; B' = NH; X = IV; U'W' = 3-SO2N[(CH2)2CONH2]2} which showed IC50 of 0.3 .mu.G/mL against respiratory syncytial virus growth.

IT **197366-24-8P 197366-84-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of bis-aryloxy(amino)-triazinyl-oxy(amino)aryl derivs. as antiviral agents)

RN 197366-24-8 CAPLUS
CN [1,1'-Biphenyl]-2,2'-disulfonic acid, 4,4'-bis[[4,6-bis[[3-[[bis(2-amino-2-oxoethyl)amino]sulfonyl]phenyl]amino]-1,3,5-triazin-2-yl]amino]-, disodium salt (9CI) (CA INDEX NAME)

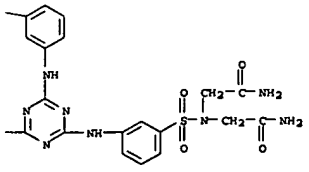
L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



●2 Na

PAGE 1-B



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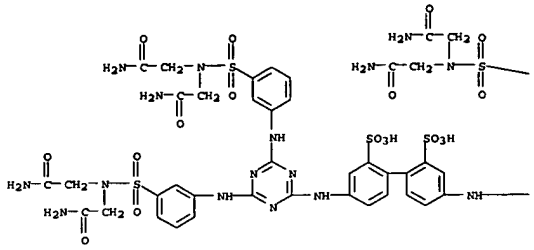
L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN (Continued)

PAGE 1-A



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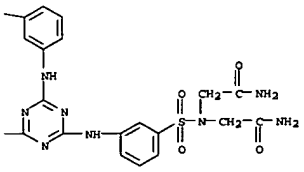

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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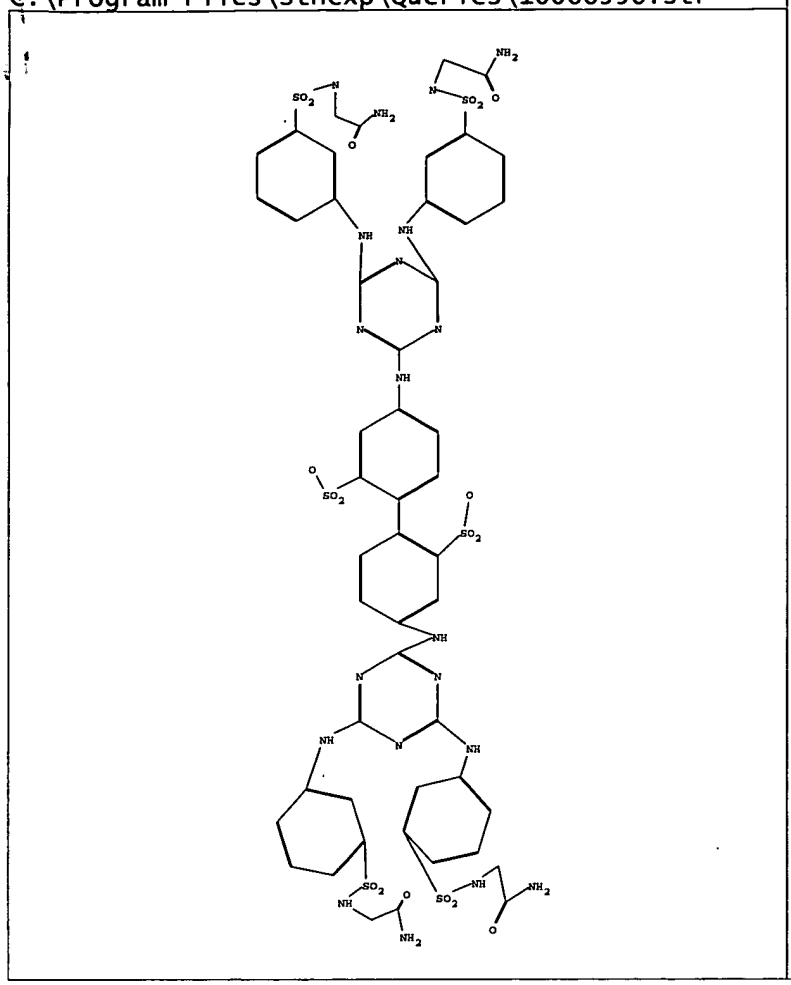

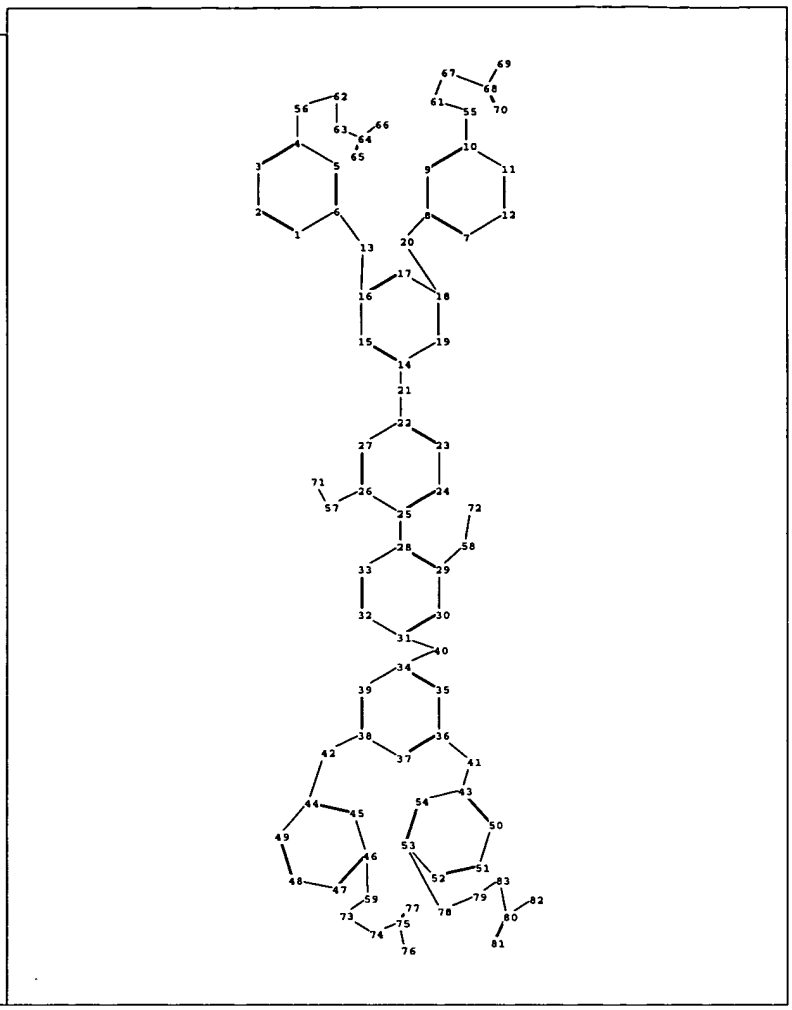

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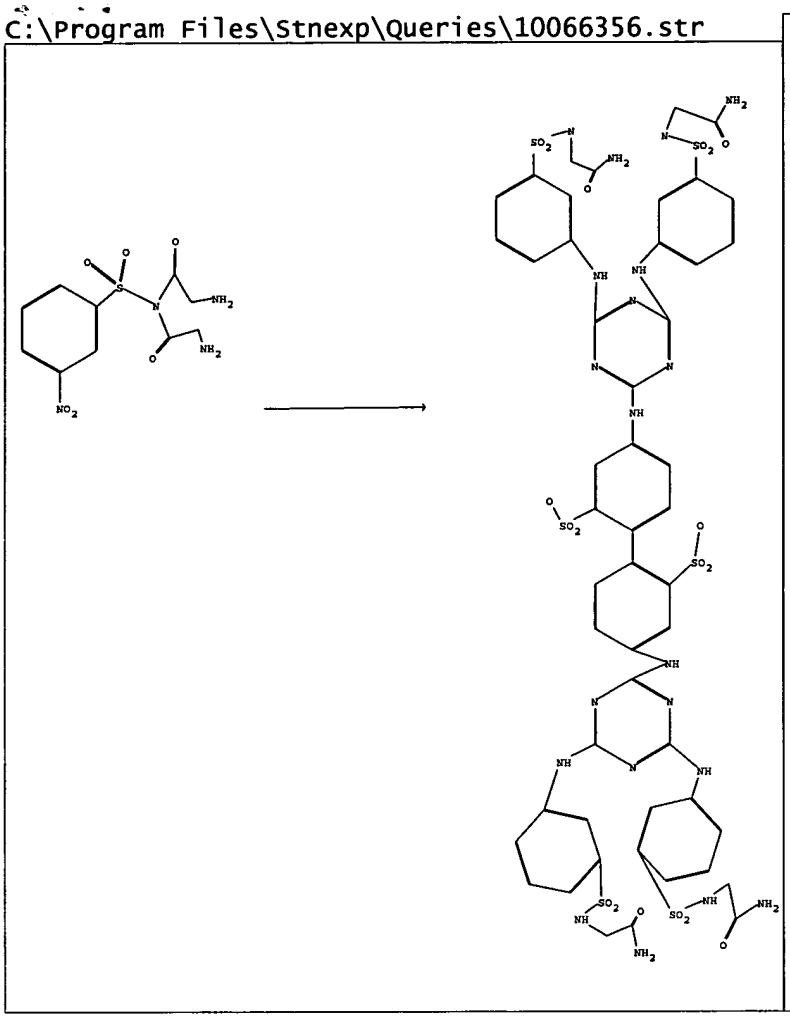

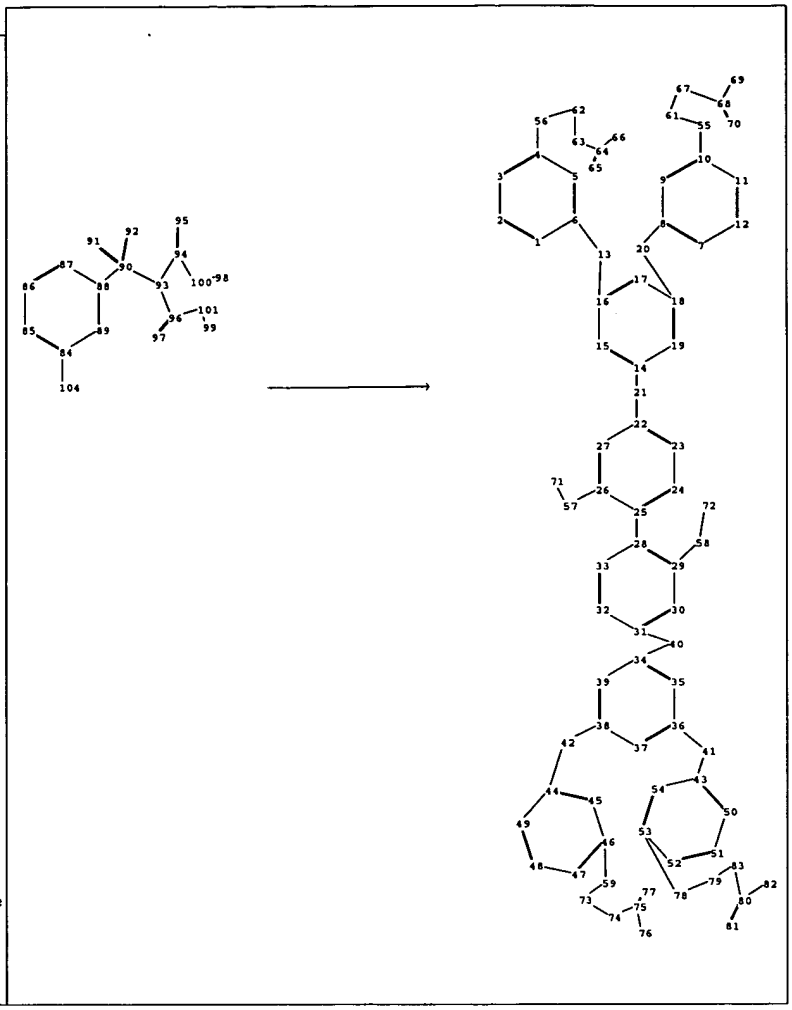

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ring nodes :
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96-101 98-100 99-101
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 14-15 14-19 15-16
16-17 17-18 18-19 22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31
31-32 32-33 34-39 34-35 35-36 36-37 37-38 38-39 43-50 43-54 44-45 44-49 45-46
46-47 47-48 48-49 50-51 51-52 52-53 53-54 84-85 84-89 85-86 86-87 87-88 88-89
exact/norm bonds :
6-13 8-20 13-16 14-21 18-20 21-22 31-40 34-40 36-41 38-42 41-43 42-44 55-61
56-62 57-71 58-72 59-73 61-67 62-63 64-65 64-66 68-70 68-69 73-74 75-76 75-77
78-79 79-83 80-82 80-81 88-90 90-91 90-92 90-93 93-94 93-96 94-95 96-97 98-100
99-101
exact bonds :
4-56 10-55 25-28 26-57 29-58 46-59 53-78 63-64 67-68 74-75 80-83 84-104 94-100
96-101
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 14-15 14-19 15-16
16-17 17-18 18-19 22-23 22-27 23-24 24-25 25-26 26-27 28-29 28-33 29-30 30-31
31-32 32-33 34-39 34-35 35-36 36-37 37-38 38-39 43-50 43-54 44-45 44-49 45-46
46-47 47-48 48-49 50-51 51-52 52-53 53-54 84-85 84-89 85-86 86-87 87-88 88-89
isolated ring systems :
containing 7 : 22 : 28 : 43 : 44 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS
22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom
32:Atom 33:Atom 34:Atom 35:Atom 36:Atom 37:Atom 38:Atom 39:Atom 40:CLASS 41:CLASS
42:CLASS 43:Atom 44:Atom 45:Atom 46:Atom 47:Atom 48:Atom 49:Atom 50:Atom 51:Atom
52:Atom 53:Atom 54:Atom 55:CLASS 56:CLASS 57:CLASS 58:CLASS 59:CLASS 61:CLASS
62:CLASS 63:CLASS 64:CLASS 65:CLASS 66:CLASS 67:CLASS 68:CLASS 69:CLASS 70:CLASS
71:CLASS 72:CLASS 73:CLASS 74:CLASS 75:CLASS 76:CLASS 77:CLASS 78:CLASS 79:CLASS
80:CLASS 81:CLASS 82:CLASS 83:CLASS 84:Atom 85:Atom 86:Atom 87:Atom 88:Atom
89:Atom 90:CLASS 91:CLASS 92:CLASS 93:CLASS 94:CLASS 95:CLASS 96:CLASS 97:CLASS
98:CLASS 99:CLASS 100:CLASS 101:CLASS 104:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 84

FILE 'REGISTRY' ENTERED AT 17:00:25 ON 20 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 OCT 2003 HIGHEST RN 606921-26-0
DICTIONARY FILE UPDATES: 19 OCT 2003 HIGHEST RN 606921-26-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10066356.str

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.80	1.01

FILE 'CASREACT' ENTERED AT 17:01:19 ON 20 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1907 - 19 Oct 2003 VOL 139 ISS 16

Some records from 1974 to 1991 are derived from the ZIC/VINITI data file and provided by InfoChem and some records are produced using some INPI data from the period prior to 1986.

This file contains CAS Registry Numbers for easy and accurate substance

identification.

Crossover limits have been increased. See HELP RNCROSSOVER for details.

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

```
=> s l1
SAMPLE SEARCH INITIATED 17:01:23 FILE 'CASREACT'
SCREENING COMPLETE -      0 REACTIONS TO VERIFY FROM      0 DOCUMENTS

100.0% DONE      0 VERIFIED       0 HIT RXNS                      0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:         0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1 (     0 REACTIONS)

=> s l1 sss full
FULL SEARCH INITIATED 17:01:31 FILE 'CASREACT'
SCREENING COMPLETE -      0 REACTIONS TO VERIFY FROM      0 DOCUMENTS

100.0% DONE      0 VERIFIED       0 HIT RXNS                      0 DOCS
SEARCH TIME: 00.00.01

L3            0 SEA SSS FUL L1 (     0 REACTIONS)

=> log y
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                  97.85      98.86

STN INTERNATIONAL LOGOFF AT 17:01:37 ON 20 OCT 2003
```